

Applicant: Cy A. Stein et al.
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Page 2

A'
NO:9), J (SEQ ID NO:10), K (SEQ ID NO:11), L (SEQ ID NO:12), M (SEQ ID NO:13). --

Please replace the Figure description starting at page 5, line 5 with the following rewritten Figure description:

-- Figures 2A and 2B

A²
Oligonucleotide sequences and analogs thereof complementary to bcl-X_L mRNA; Figure 2A shows: A (SEQ ID NO:14), A' (SEQ ID NO:15), B (SEQ ID NO:16), C (SEQ ID NO:17), C' (SEQ ID NO:18), D (SEQ ID NO:19), E (SEQ ID NO:20), E' (SEQ ID NO:21), F (SEQ ID NO:22), G (SEQ ID NO:23), G' (SEQ ID NO:24); Figure 2B shows, H (SEQ ID NO:25), H' (SEQ ID NO:26), I (SEQ ID NO:27), I' (SEQ ID NO:28), J (SEQ ID NO:29), K (SEQ ID NO:30), K' (SEQ ID NO:31), L (SEQ ID NO:32), L' (SEQ ID NO:33), M (SEQ ID NO:34), M' (SEQ ID NO:35). --

Please replace the Figure description starting at page 6, line 2 with the following rewritten Figure description:

-- Figure 10

A³
Most active chimeric PS-PO oligonucleotides by their ability to down-regulate Bcl-XL protein expression (from top to bottom SEQ ID NO:15; SEQ ID NO:19; SEQ ID NO:24; SEQ ID NO:27; SEQ ID NO:22; SEQ ID NO:29; and SEQ ID NO:38). --

In the Specification:

Please replace the paragraph starting page ²³22, line ¹⁷33 with the following rewritten paragraph:

A⁴
- Two clones of LNCaP cells overexpressing bcl-xL protein (1072-4 and 1072-5) have been obtained after transfection of wild type LNCaP cells with the plasmid vector pSFFV/bcl-xL and lipofectin. Also a mock transfectant clone of LNCaP cells carrying neo[®] resistance gene (1072-3) was used for the control experiments. Clone 1072-4 demonstrates 10-fold overexpression, and clone 1072-5 - 4-fold overexpression of bcl-xL protein. Western blot analysis for bcl-xL protein was performed as described above. Results for bcl-xL protein expression were confirmed by Northern blot analysis for bcl-xL mRNA expression, demonstrating significant elevation of this mRNA in bcl-xL transformed cell lines. For the Northern blot analysis, the total RNA was isolated from the cells using TRIZOL reagent (GIBCO BRL), and 20 µg aliquotes were separated in RNA-formaldehyde gel, blotted onto nylon membranes (Schleicher & Schull), UV-linked and prehybridized for two hours at 42 °C in the standard hybridization solution. Then the blot was hybridized overnight with the PCR-amplified fragment of human bcl-xL cDNA at 42 °C. Bcl-xL coding fragment was amplified from pSFFV/bcl-xL plasmid using bcl-x specific primers. The primer sequences were: bcl-x-upstream, 5'-ATGTCTCAGAGCAACCGGGA-3' (SEQ ID NO:36); and bcl-x-downstream, 5'-TCATTTCCGACTGAAGAGTG-3' (SEQ ID NO:37). Twenty five cycles of amplification were performed in DNA Thermal Cycler (Perkin-Elmer, Norwalk, CT) at 94 °C (30 sec), 55 °C (30 sec), and 72 °C (30 sec). The PCR products were analysed on a 1.2% agarose gel. The resultant fragment was labeled by random primer method to the specific activity 10⁷ cpm/ng of the probe and used for the hybridization. After washings blots were autoradiographed for 24h at -80 °C. Blots